

Amendments to the Claims:

The following **Listing of Claims** will replace all earlier versions and listings of the claims.

Listing of Claims:

1. ***(currently amended)*** An in vitro method for the determination of the formation of endothelins in serious diseases, in particular cardiovascular diseases, inflammations, sepsis and cancer, in whole blood, plasma or serum of a human patient suspected of a disease selected from the group consisting of cardiovascular disease, inflammation, sepsis and cancer for purposes of medical diagnostics, wherein the formation of endothelin-1 (SEQ ID NO.:2) and big endothelin-1 (SEQ ID NO.: 3) is determined by ~~determining those~~detecting a C-terminal fragments of preproendothelin-1 (SEQ ID NO.: 1) ~~which are recognized by antibodies which bind to peptides which correspond to peptide sequences in the range of amino acids 93 to 212 of preproendothelin-1~~ suspected of a disease selected from the group consisting of cardiovascular disease, inflammation, sepsis and cancer, the method comprising:
 - obtaining a whole blood, plasma or serum sample from the patient;
 - contacting said sample with first antibodies that specifically bind to a first epitope within amino acids 168-212 of preproendothelin and second antibodies that specifically bind to a second epitope within amino acids 168-212 of preproendothelin, one of said first and second antibodies being labeled with a detectable marker, wherein the level of a C-terminal fragment detected by said first and second antibodies correlates with the level of formation of endothelin-1 (SEQ ID NO:2) or big endothelin-1 (SEQ ID NO:3) in said patient.
- 2-4. ***(canceled)***

5. **(currently amended)** The method as claimed in claim 4~~1~~, wherein said first and second antibodies bind to two different regions of preproendothelin-1 selected from amino acids 168-181, 184-203 and 200-212 of preproendothelin-1 ~~for determining a C-terminal fragment comprising amino acids 168 to 212 of preproendothelin-1 (SEQ ID NO:7).~~
6. **(currently amended)** The method of claim 1, wherein said method provides for the quantitative or semiquantitative determination of ~~the peptide a C-terminal~~ fragments of preproendothelin-1 comprising amino acids 168-212 of preproendothelin-1.
7. **(currently amended)** The method as claimed in claim 6, wherein said determination is an immunochromatographic point-of-care test ~~or another accelerated test.~~
8. **(currently amended)** The method as claimed in claim 1, wherein the first and second antibodies used for the determination are selected from monoclonal antibodies, affinity-purified polyclonal antibodies, or a combination of monoclonal and affinity-purified antibodies.
9. **(currently amended)** The method as claimed in claim 1, wherein the first and second antibodies are obtained by immunizing an animal with a synthetic peptide consisting of amino acids 168-181, 184-203 or 200-212 of preproendothelin-1.
10. **(previously presented)** The method as claimed in claim 1, wherein one of said first and second antibodies is bound to a solid phase.
11. **(currently amended)** The method as claimed in claim 1, wherein ~~two said first and second antibodies are used for the determination, both of which~~ two said first and second antibodies are present in dispersed form in the liquid reaction mixture, a first ~~marking component which~~

~~is part of a marking system based on fluorescence or chemiluminescence distinction or amplification~~detectable marker being bound to the first antibody, and ~~thea second marking component of this marking system~~detectable marker being bound to the second antibody so that, after binding of both antibodies to the ~~peptide-terminal~~ fragment of preproendothelin-1 to be detected ~~to form an~~ analyte/antibody complex, a measurable signal which permits detection of the ~~resulting sandwich~~ complexes in the measuring solution is generated.

12. **(currently amended)** The method as claimed in claim 11, wherein the ~~marking system~~detectable marker comprises rare earth cryptates or chelates in combination with a fluorescent or chemiluminescent dye, ~~in particular of the cyanine type.~~
13. **(currently amended)** The method as claimed in claim 1, ~~which is used for diagnosis, for determination of severity and for prognosis and for monitoring the therapy in the course of~~wherein said disease is sepsis.
14. **(original)** The method as claimed in claim 13, which is carried out as part of a multiparameter determination, in which at least one further parameter relevant to sepsis diagnosis is determined simultaneously.
15. **(original)** The method as claimed in claim 14, wherein the further parameter or parameters relevant for sepsis diagnosis is or are selected from the group which consists of anti-ganglioside antibodies, the proteins calcitonin, CA 125, CA 19-9, S100B, S100A proteins, LASP-1, soluble cytokeratin fragments, in particular CYFRA 21, TPS and/or soluble cytokeratin-1 fragments (sCY1F), the peptides inflammin and CHP, fragments of the prohormones pro-ANP, pro-BNP or pro-ADM, glycine-N-acyltransferase (GNAT), carbamoylphosphate synthetase 1 (CPS 1) and C-reactive protein (CRP) or fragments thereof.
16. **(currently amended)** The method as claimed in claim 1, ~~which is used in the area of cardiac diagnostics~~wherein said disease is cardiovascular disease.

17. **(currently amended)** The method as claimed in claim 16, which is carried out as part of a multiparameter determination, in which further parameters relevant to ~~cardiac diagnostics~~cardiovascular disease are determined simultaneously.
18. **(currently amended)** The method as claimed in claim 1, ~~which is used in the area of~~wherein said disease is cancer ~~diagnostics~~.
19. **(original)** The method as claimed in claim 18, which is carried out as part of a multiparameter determination, in which further parameters relevant to cancer ~~diagnostics~~ are determined simultaneously.
20. **(withdrawn)** An antibody which binds specifically to peptides which consist of the amino acid sequences which correspond to the amino acids 168-181, 184-203 and 200-212 of preproendothelin-1.
21. **(withdrawn)** The antibody as claimed in claim 20, which is an affinity-purified polyclonal antibody or monoclonal antibody.
22. **(withdrawn)** A kit for carrying out a method as claimed in claim 1, which comprises at least: (a) a first antibody as claimed in either of claims 20 and 21, (b) a second, different antibody as claimed in either of claims 20 and 21, one of the antibodies being marked and the other being immobilized or immobilizable, and (c) a standard peptide which has an amino acid sequence which comprises at least the amino acids 168-203 or 168-212 of preproendothelin.
23. **(withdrawn)** The kit as claimed in claim 22, wherein the immobilized antibody is present in immobilized form on the walls of a test tube (CT).

24. *(new)* A method for determining the level of endothelin formation in a human patient suspected of a disease selected from the group consisting of cardiovascular disease, inflammation, sepsis and cancer, wherein the level of endothelin formation is determined by measuring the level of a C-terminal fragment of preproendothelin-1, the method comprising:
- obtaining a whole blood, plasma or serum sample from the patient;
 - contacting said sample with first antibodies that specifically bind to a first epitope within amino acids 168-212 of preproendothelin and second antibodies that specifically bind to a second epitope within amino acids 168-212 of preproendothelin, one of said first and second antibodies being labeled with a detectable marker; and
 - measuring the level of a C-terminal fragment of preproendothelin detected by said first and second antibodies, wherein the level of C-terminal fragment detected by said first and second antibodies correlates with the level of endothelin-1 formation in said patient.